Terminal Disclaimer terminally disclaiming the portion of any patent issuing herein that would extend beyond the expiration of the Boyce et al. patent.

Claim 10 has been amended to change its dependency to Claim 9 in order to conform to what was originally intended.

The Examiner has rejected Claims 1-11, 13, 14, 19-23, 34-45, 56-63, 74-82 and 93-94 under 35 U.S.C. §102(b) for anticipation by Lyle U.S. Patent No. 5,061,286 ("Lyle"). According to the Examiner, Lyle discloses demineralized bone particles (which, of course, possess surface-exposed collagen) that are "linked together" with a binder such as cyanoacrylate.

The Examiner's rejection is believed to be totally without merit.

While the Lyle demineralized bone particles possess surface-exposed collagen, there is not the slightest hint anywhere in this disclosure of the demineralized bone particles being "bonded to each other through chemical linkages between their surface-exposed collagen". Undoubtedly, the Lyle demineralized bone particles possess surface-exposed collagen. Undoubtedly, the Lyle binding agents, e.g., cyanoacrylate of which the Examiner has taken particular note, binds the demineralized bone particles together. However, the function of cyanoacrylate in Lyle (and that of all the other binding agents disclosed in the patent) is essentially that of an adhesive*. There is no disclosure or suggestion of the Lyle binding agent chemically modifying the surface exposed collagen of the demineralized bone

* It is, of course, to be understood that "cyanoacrylate" as disclosed in Lyle is not an adhesive but a monomer which, when polymerized, provides the actual adhesive. This is abundantly clear from the attached copy of the article "2-Cyanoacrylic Ester Polymers" ("Encyclopedia of Polymer Science and Engineering", Volume 1, pages 299-305(Wiley, 1985).

particles such that chemical linkages are formed between the surface-exposed collagen of adjacent demineralized bone particles. In lacking any disclosure or suggestion of such chemical linkages, Lyle fails to anticipate or render obvious the subject matter of any of Claims 1-94.

The Examiner has rejected Claims 1-5, 7, 11-14, 16, 19-21, and 34-35 under 35 U.S.C. §102(b) for anticipation by Jefferies U.S. Patent No. 4,394,370 ("Jefferies").

According to the Examiner, Jefferies discloses demineralized bone particles whose surface-exposed collagen is crosslinked thereby inherently improving the mechanical strength of the resulting product, a grafting implant capable of inducing the formation of new bone in an animal in which it is implanted.

Even if the foregoing characterization of the Jefferies disclosure is considered to be essentially accurate, the invention of the claims as amended herein is believed to be both novel and unobvious over Jefferies.

Claim 1 and all of the remaining claims presented herein now recite that where *substantially all* of the bone-derived elements are substantially completely demineralized bone-derived elements (as recited in amended Claim 3), the osteoimplant contains at least one additional component selected from the group consisting of reinforcing particles and fillers. The Jefferies demineralized bone particles are substantially completely demineralized bone particles, i.e., they contain little if any of their original mineral content, primarily made up of calcium compounds. In lacking any appreciable quantity of their original mineral content, substantially completely demineralized bone particles no longer possess the mechanical strength properties that are characteristic of whole bone (i.e., fully mineralized bone) and to a

somewhat lesser but still meaningful extent, superficially demineralized bone. This being the case, the Jefferies grafting implant, even assuming its substantially demineralized bone particles are bonded to each other through chemical linkages, would nevertheless lack any significant mineral content as would elevate its mechanical strength beyond that of the aggregated demineralized bone particles themselves. Jefferies neither discloses nor suggests incorporating into the grafting implant any component which would improve the mechanical properties of the aggregated demineralized bone particles.

In contrast to the Jefferies grafting implant, the osteoimplant of this invention contains at least one mechanical strength-imparting component. That component can be superficially demineralized bone in which case no additional mechanical strength-imparting component is required or, when substantially all of the bone-derived elements in the osteoimplant are substantially completely demineralized (as in the Jefferies grafting implant), reinforcing particles and/or fillers must be incorporated therein. As previously noted, there is not the slightest suggestion in Jefferies of incorporating a reinforcing component of any kind into the grafting implant. In point of fact, this is not a concern of Jefferies. Jefferies is concerned with repairing bone defects by inducing new bone growth at a bone repair site. Demineralized bone powder with its osteogenic capability satisfies this concern. However, it is clear that the Jefferies grafting implant is not intended to be used in circumstances where it can be expected to sustain relatively high mechanical loads. Thus, at column 2, lines 39-45, Jefferies discloses that implants according to the invention (referred to in the cited passage as "complexes") can be made into "thin membranes", "gels" or "preferably in

a sponge-like configuration". These final products by their very nature are not intended to withstand high mechanical stresses. In contrast to these Jefferies products, applicants' osteoimplant as recited in the amended claims must possess some component which, in effect, imparts mechanical strength to crosslinked bone elements which is above and beyond that of merely crosslinked substantially completely demineralized bone elements. As previously stated, this mechanical strength-supporting component can be provided by the mineral content of superficially demineralized bone-derived elements (when such are employed) or when such mineral content is absent, or nearly absent, some added reinforcing particles/fillers. Due to this arrangement, applicants' osteoimplant can be used to repair or replace a variety of bones where mechanical strength of the osteoimplant is a practical consideration. See, for example, the disclosure at pages 13 and 14 of the specification.

In view of the foregoing, amended Claims 1-92 are believed to be both novel and nonobvious over the Jefferies disclosure.

The Examiner has rejected Claims 12 and 15-18 under 35 U.S.C. §103(a) for obviousness over Lyle. The Examiner characterizes Lyles' "cyanoacrylate" as a crosslinking agent. However, as noted above in connection with the Examiner's rejection of the claims for supposed anticipation by Lyle, cyanoacrylate is a monomer which provides a polymer, the polymer being the actual adhesive which binds the Lyle demineralized bone particles together. There is no disclosure or suggestion in Lyle that cyanoacrylate functions in any other way.

In the absence of any indication in Lyle that the demineralized bone particles therein are bonded to each other through chemical bonds formed in their collagen-exposed surfaces, amended Claims 1-92 can only be regarded as nonobvious, and therefore patentable, over Lyle.

Applicants have taken note of the Examiner's willingness to allow certain claims (i.e., Claims 24-32, 46-54, 64-72, 83-91, 33, 55, 73 and 92) if rewritten in the ways proposed by the Examiner. In view of the amendment of Claims 1-92 and traverse of the prior art rejections presented herein, applicants believe that all of the amended claims are in form for allowance, formal notification thereof being respectfully requested.

Respectfully submitted,

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MARKED UP VERSION OF THE AMENDED CLAIMS

The following amendments are made:

1. (Amended) An osteoimplant which comprises a solid aggregate of bone-derived elements selected from the group consisting of superficially demineralized bone-derived elements, substantially completely demineralized bone-derived elements and mixtures thereof, adjacent bone-derived elements being bonded to each other through chemical linkages between their surface-exposed collagen, provided, that where substantially all of the bone-derived elements are substantially completely demineralized bone-derived elements the osteoimplant contains at least one additional component selected from the group consisting of reinforcing particles and fillers.

2. (Amended) The osteoimplant of Claim 1 wherein substantially all of the bone-derived elements are superficially demineralized particles, strips or sheets of allogenic, xenogenic cortical [and/] or cancellous bone.

3. (Amended) The osteoimplant of Claim 1 wherein substantially all of the bone-derived elements are substantially completely demineralized particles, strips or sheets of allogenic, xenogenic cortical [and/] or cancellous bone, the reinforcing particles being selected from the group consisting of fully mineralized bone, graphite and pyrolytic carbon.

4. (Amended) The osteoimplant of Claim 1 [containing at least one other component] wherein substantially all of the bone-derived elements are substantially completely demineralized particles, strips or sheets of allogenic, xenogenic cortical or cancellous bone, the filler being selected from the group consisting of hydroxyapatite, tricalcium phosphate, other calcium salts, bioglass, bioceramic, bioabsorbable polymer, nonbioabsorbable material and mixtures thereof.

5. (Amended) The osteoimplant of Claim [4 wherein the component is] 1 containing an additional component selected from the group consisting of [reinforcing particle or fiber, filler,] bone-growth inducing substance, growth factors, [fully mineralized allogenic or xenogenic bone,] cellular material, genetic material, calcification-controlling agent[,] and hydration agent[, inorganic compounds and polymers].

10. (Amended) The osteoimplant of Claim [1] 9 wherein the hydration-facilitating agent is glycerol.

11. (Amended) [An osteoimplant which comprises a solid aggregate of bone-derived elements, adjacent bone-derived elements being bonded to each other through chemical linkages between their surface-exposed collagen,] The osteoimplant of Claim 1 wherein the chemical linkages are formed by exposing the bone-derived elements to a chemical crosslinking agent.

19. (Amended) The osteoimplant of Claim 11 wherein substantially all of the bone-derived elements are superficially demineralized particles, strips or sheets or allogenic, xenogenic cortical or cancellous bone.

20. (Amended) The osteoimplant of Claim 11 [further comprising at least one other component] wherein substantially all of the bone-derived elements are substantially completely demineralized particles, strips or sheets of allogenic, xenogenic cortical [and/] or cancellous bone, the reinforcing particles being selected from the group consisting of fully mineralized bone, graphite and pyrolytic carbon.

21. (Amended) The osteoimplant of Claim [20 wherein the component is] 11 containing an additional component selected from the group consisting of [reinforcing particles, reinforcing fibers, filler,] bone-growth inducing substances, growth factors, [fully mineralized bone,] adhesives, plasticizers, flexibilizing agents, cellular material, genetic material, calcification-controlling agents, hydration facilitating agents, biostatic agents, biocidal agents, polymers, inorganic compounds, substances imparting radiopacity and metallic meshes.

24. (Amended) The osteoimplant of Claim 11 wherein the bone-derived elements are superficially demineralized or substantially fully demineralized sheets obtained by longitudinally slicing the diaphyseal region of whole cortical bone.

33. (Amended) The osteoimplant of Claim 24 configured and dimensioned as an intervertebral insert, a long bone, a cranial bone, a bone of the pelvis, [or] a bone of the hand [or], a bone of the foot or section [thereof] of any of the foregoing.

35. (Amended) The osteoimplant of Claim 34 [wherein the pores, perforations, apertures, channels or spaces have] having incorporated therein one or more bone growth inducing or bone healing substances.

36. (Amended) [An osteoimplant which comprises a solid aggregate of bone-derived elements, adjacent bone-derived elements being bonded to each other through chemical linkages between their surface-exposed collagen,] The osteoimplant of Claim 1 wherein the chemical linkages are formed by application of energy.

41. (Amended) The osteoimplant of Claim 36 wherein substantially all of the bone-derived elements are superficially demineralized particles, strips or sheets of allogenic, xenogenic cortical or cancellous bone.

42. (Amended) The osteoimplant of Claim 36 [further comprising at least one other component] wherein substantially all of the bone-derived elements are substantially completely demineralized particles, strips or sheets of allogenic, xenogenic cortical [and/] or cancellous bone, the reinforcing particles being selected from the group consisting of fully mineralized bone, graphite and pyrolytic carbon.

43. The osteoimplant of Claim [42 wherein the component is] 36 containing an additional component selected from the group consisting of [reinforcing particles, reinforcing fibers, fillers,] bone-growth inducing substances, growth factors, [fully mineralized bone,] adhesives, plasticizers, flexibilizing agents, cellular material, genetic material, calcification-controlling agents, hydration facilitating agents, biostatic agents, biocidal agents, polymers, inorganic compounds, substances imparting radiopacity and metallic meshes.

55. (Amended) The osteoimplant of Claim 46 configured and dimensioned as an intervertebral insert, a long bone, a cranial bone, a bone of the pelvis, [or] a bone of the hand [or], a bone of the foot or section [thereof] of any of the foregoing.

58. (Amended) [An osteoimplant which comprises a solid aggregate of bone-derived elements, adjacent bone-derived elements being bonded to each other through chemical linkages between their surface-exposed collagen,] The osteoimplant of Claim 1 wherein the chemical linkages are formed by dehydrothermal treatment.

59. (Amended) The osteoimplant of Claim 58 wherein substantially all of the bone-derived elements are superficially demineralized particles, strips or sheets of allogenic, xenogenic cortical or cancellous bone.

60. (Amended) The osteoimplant of Claim 58 [further comprising at least one other component] wherein substantially all of the bone-derived elements are substantially completely demineralized particles, strips or sheets of allogenic, xenogenic cortical [and/] or cancellous bone, the reinforcing particles being selected from the group consisting of fully mineralized bone, graphite and pyrolytic carbon.

61. (Amended) The osteoimplant of Claim [60 wherein the component is] 58 containing an additional component selected from the group consisting of [reinforcing particles, reinforcing fibers, fillers,] bone-growth inducing substances, growth factors, [fully mineralized bone,] adhesives, plasticizers, flexibilizing agents, cellular material, genetic material, calcification-controlling agents, hydration facilitating agents, biostatic agents, biocidal agents, polymers, inorganic compounds, substances imparting radiopacity and metallic meshes.

73. (Amended) The osteoimplant of Claim 64 configured and dimensioned as an intervertebral insert, a long bone, a cranial bone, a bone of the pelvis, [or] a bone of the hand [or], a bone of the foot or section [thereof] of any of the foregoing.

76. (Amended) [An osteoimplant which comprises a solid aggregate of bone-derived elements, adjacent bone-derived elements being bonded to each other through chemical linkages between their surface-exposed collages,] The osteoimplant of Claim 1 wherein the chemical linkages are formed by enzymatic treatment.

78. (Amended) The osteoimplant of Claim 76 wherein substantially all of the bone-derived elements are superficially demineralized particles, strips or sheets of allogenic, xenogenic cortical or cancellous bone.

79. (Amended) The osteoimplant of Claim 76 [further comprising at least one other component] wherein substantially all of the bone-derived elements are substantially completely demineralized particles, strips or sheets of allogenic, xenogenic cortical [and/] or cancellous bone, the reinforcing particles being selected from the group consisting of fully mineralized bone, graphite and pyrolytic carbon.

80. (Amended) The osteoimplant of Claim [79 wherein the component is] 76 containing an additional component selected from the group consisting of [reinforcing particles, reinforcing fibers, fillers,] bone-growth inducing substances, growth factors, [fully mineralized bone,] adhesives, plasticizers, flexibilizing agents, cellular material, genetic material, calcification-controlling agents, hydration facilitating agents, biostatic agents, biocidal agents, polymers, inorganic compounds, substances imparting radiopacity and metallic meshes.

92. (Amended) The osteoimplant of Claim 83 configured and dimensioned as an intervertebral insert, a long bone, a cranial bone, a bone of the pelvis, [or] a bone of the hand [or], a bone of the foot or section [thereof] of any of the foregoing.

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2-CYANOACRYLIC ESTER POLYMERS

2-Cyanoacrylic ester polymers provide excellent adhesive bonds between a wide variety of substrates. These polymeric bonds are formed rapidly at room temperature and without the addition of a catalyst by spreading a monomeric cyanoacrylic ester, $CH_2{=}C(CN)COOR$, into a thin film that joins two adherends. This unique behavior was discovered in 1951 in the Research Laboratories at Tennessee Eastman Co. during the course of basic research directed toward characterizing polymers derived from 1,1-disubstituted ethylenes. Following the preparation of a fresh sample of ethyl 2-cyanoacrylate, a routine measurement of

refractive index was made. Upon completion, the chemist performing this measurement was startled to find that he could not separate the refractometer's prisms. Within hours, the full implication of these adhered prisms was apparent, as fast-setting bonds were obtained between several different substrates (1–7). This discovery led to the introduction in 1958 of Eastman 910 adhesive, the first commercial 2-cyanoacrylic ester adhesive. Similar adhesive compositions (qv) have been marketed under such brand names as Permabond, Super Glue, and Krazy Glue, and because of their unique performance, have been used in a broad spectrum of industrial, consumer, and medical adhesive applications.

Physical Properties

The industrially important 2-cyanoacrylic ester adhesives are usually prepared from methyl, ethyl, allyl, or butyl 2-cyanoacrylate; ethyl 2-cyanoacrylate is the most commonly used monomer. These 2-cyanoacrylic esters are formulated into a variety of adhesives having viscosities from 2 mPa·s (mPa·s = cP) to about 3000 mPa·s. This range of viscosities facilitates the handling and application of the adhesives. Viscosity also affects gap-filling capability; the more viscous formulations form bonds across gaps as large as 375 μm (0.015 in.). However, the strongest bonds are usually obtained when bond thickness is less than 50 μm (0.002 in.). The set times of 2-cyanoacrylic ester adhesives are usually less than 2 min on most substrates; lower viscosity formulations form bonds two to five times faster than more viscous compositions. Set times also generally increase as the gap increases. In recent years, the use of surface activators or primers has broadened the utility of 2-cyanoacrylic ester adhesives by accelerating their polymerization on most surfaces and speeding bond formation across larger gaps.

2-Cyanoacrylic ester adhesives generally achieve sufficient bond strength to permit handling of the bonded substrates in 10 min or less. Shear strengths on steel, aluminum, and copper substrates are usually in the 10–25 mPa (1400–3600 psi) range after 48 h. The 2-cyanoacrylic ester adhesives also give excellent bond strength on most plastic and rubber substrates. For example, 23 different kinds of 2-cyanoacrylic ester adhesives on plastic-to-plastic substrates gave the average shear strengths, ie, three lapshear bonds per adhesive, listed in Table 1.

It is generally difficult to get good bonds on polyethylene, polypropylene, or Teflon fluorocarbon resin, which are important plastics not shown in Table 1. Bonds of good strength, often greater than that of the substrates, can also be obtained with 2-cyanoacrylic esters on wood, but special techniques may be required to get good bond strength on very porous substrates (6–10).

The physical properties of bonds of 2-cyanoacrylic ester polymers are affected by moisture, heat, and solvents. These bonds deteriorate in moisture, but the deterioration is usually not rapid enough to detract from the bonds' usefulness in many applications. Bonds between rubber-to-rubber, rubber-to-metal, and rubber-to-plastic substrates have generally maintained useful strengths after weathering (qv) outdoors for several years. However, bonds between metals, rigid plastics, and glass rapidly deteriorate in moisture. Since most 2-cyanoacrylic ester polymers begin degrading at temperatures above ca 70°C, they should not be used in applications where they will be subjected to these temperatures for a long

Table 1. Average Shear Strengths for 2-Cyanoacrylic Ester Adhesives on Plastic-to-Plastic Substrates

Plastic type	Shear strength, MPa (psi)
acrylic	3.8 (550)[a]
acrylonitrile–butadiene–styrene	5.8 (840)[a]
cellulose acetate butyrate	2.6 (380)[a]
nylon	2.8 (410)
nylon, glass-filled	5.7 (830)
phenolic	9.0 (1310)[a]
acetal	1.5 (220)
polycarbonate	8.6 (1250)[a]
polyester	1.3 (190)
polyester, glass-filled	1.4 (200)
polystyrene	3.0 (430)[a]
polysulfone	4.1 (600)[a]
rigid vinyl	5.4 (790)[a]

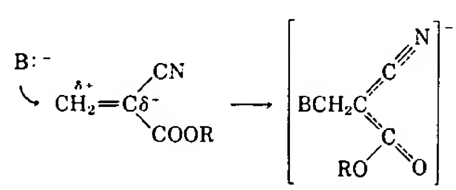
[a] Bond held, but a substantial number of substrates broke.

time. However, an adhesive, probably based on allyl 2-cyanoacrylate, reportedly gives bonds that will withstand 200–250°C temperatures (6). Bonds of 2-cyanoacrylic ester adhesives have good resistance to many solvents, but they are substantially weakened by dilute alkaline solutions, dilute acid solutions, acetone, nitromethane, dimethylsulfoxide, and *N,N*-dimethylformamide, as well as water.

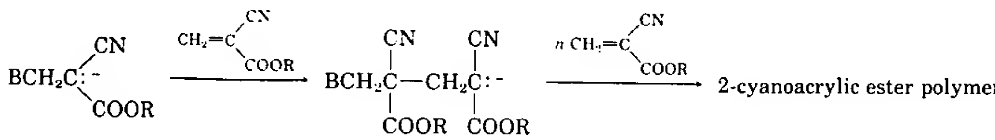
The excellent adhesion that 2-cyanoacrylic esters have to skin has been used to develop surgical adhesives as replacements for sutures and as hemostatic agents. Although not currently approved for this use in the United States, compositions prepared from butyl 2-cyanoacrylate, isobutyl 2-cyanoacrylate, and ethyl 2-cyanoacrylate are in use in other parts of the world. Because these compositions exhibit good wetting properties on tissue, form a protective coating over damaged tissue, and provide bonds having strengths greater than that of the tissue, they provide the medical professions with unique and sometimes lifesaving capabilities.

Chemical Properties

The most important chemical property of 2-cyanoacrylic esters is their ability to form strong adhesive bonds rapidly. This property is derived from the highly electronegative configuration of the nitrile (—CN) and the alkoxycarbonyl (—COOR) groups. This enables ready addition to the polarized carbon–carbon double bond by weak bases derived from water or alcohols and resonance stabilization of the anion:



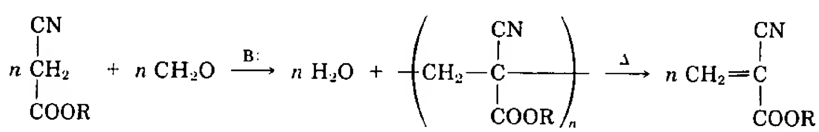
Propagation to a high molecular-weight polymer then occurs through this carbanion:



The initiation of 2-cyanoacrylic ester polymerization by nondissociated base species, sometimes used as surface-active agents, leads to a slightly different mechanism than shown. A zwitterion-type species is involved in a complex initiation followed by anionic propagation (11,12).

Manufacture and Formulation

Although there are numerous routes described in the literature for preparing cyanoacrylic esters, most syntheses involve condensing an alkyl cyanoacetate with formaldehyde in the presence of base catalyst to yield a low molecular-weight cyanoacrylic ester polymer. This polymer is then depolymerized at a high temperature to yield the 2-cyanoacrylic ester as shown (13):



Numerous improvements in this batch process have been directed toward increasing the yield and improving the stability of the cyanoacrylic ester product. These include using an organic solvent to facilitate the removal of water from the condensation reaction, using high-boiling, heat-transfer media during depolymerization (qv), controlling the cyanoacetate–formaldehyde ratio to obtain a more readily processed and depolymerized polymer intermediate, neutralizing the base catalyst and removing the resultant undesirable residue, and processing the product in a dry atmosphere to keep the water concentration below 200 ppm (14–18). Several other modifications of this condensation–depolymerization process have been described (19–27), and a novel synthesis of biscyanoacrylates has also been detailed (28). Other synthetic routes to cyanoacrylic ester have been reported, but they are not in commercial use (29–31).

Although 2-cyanoacrylic esters are useful in many applications as the unmodified monomer, they are usually formulated with one or more stabilizers, thickeners, plasticizers, and colorants to improve their use as adhesives. Both anionic and free-radical inhibitors are used to stabilize these monomers, regulate adhesive activity, and increase shelf life. Common anionic inhibitors include phosphorus pentoxide, phosphoric acid, nitric oxide, sulfur dioxide, and propane sultone (1,13,32,33). Free-radical inhibitors include hydroquinone, catechol, and derivatives of these compounds (15). The viscosity of 2-cyanoacrylic esters is often increased to improve application properties. Polymethacrylates, cellulose esters, and poly(2-cyanacrylic esters) are the most widely used viscosity regulators (1,32–35). The use of more rubbery viscosity regulators has enhanced the tough-

ness of 2-cyanoacrylic ester bonds. Plasticizers and colorants are not widely used in these adhesives, but plasticizers (qv) that are employed to improve flexibility of the adhesive bond include aliphatic monoesters, dialkyl esters of aliphatic dicarboxylic acids, trialkyl phosphates, triaryl phosphates, dialkyl alkylphosphonates, and alkyl phthalates (32). Colorants (qv) are used to increase perceptibility and are usually selected from the anthraquinone class of dyes (36,37).

Economic Aspects

The world production of 2-cyanoacrylic esters for industrial, consumer, and medical adhesive applications is estimated at 500,000 kg/yr at prices ranging from about \$30/kg to over \$1,000/kg. Total world market for 2-cyanoacrylic esters probably exceeds \$100 $\times$ 10^6/yr. Pricing is very sensitive to volume and use.

Specifications and Standards

Although 2-cyanoacrylic ester adhesives were initially sold in a limited number of general-purpose grades based on methyl and ethyl 2-cyanoacrylates, the growth in the markets for these fast-setting adhesives has led to a proliferation of special-performance adhesives in the industrial area. These special performances include graduated strengths, high temperature resistance, and improved impact. Consumer products are mostly of the general-purpose grades. U.S. government purchases are based on MIL No. A-46050.

2-Cyanoacrylic ester adhesives should be protected from the deteriorating effects of moisture, light, and heat. This is achieved by packaging the adhesive in either a plastic container with low moisture permeability and opacity or translucency, or in a metal container. Because of the high reactivity of 2-cyanoacrylic esters, these containers must have inert surfaces; otherwise, the containers might become swollen by these powerful solvents.

The method of applying adhesive must also be considered in container selection. Mechanical and pneumatic dispensing devices are available for 2-cyanoacrylic ester adhesives. This equipment can accurately meter the quantity of adhesive applied to the bond site, which provides for more consistent bond strengths and reduces waste associated with manual dispensing (see BONDING in ADHESION AND BONDING).

Analytical and Test Methods

Modern analytical chemistry has provided a number of techniques for characterizing cyanoacrylic esters, additives, and impurities. However, in addition, most products are subjected to performance tests designed to represent applications requirements. These tests may include speed-of-bond formation and bond strength on selected substrates. Accelerated shelf-life tests may be included in the product approval procedures as well.

Health and Safety Factors

2-Cyanoacrylic ester adhesives have pungent, unpleasant odors and may be mildly lacrimatory. The TLV for methyl 2-cyanoacrylate is 2 ppm (8 mg/m^3) (38). Ventilation should be provided to keep concentrations of vapor below this level. Eye and skin contact should be prevented by appropriate protective measures. If contact occurs, the area affected should be flushed with copious quantities of water; medical attention may be needed (39).

All 2-cyanoacrylic ester adhesives are defined as combustible liquids by the National Fire Protection Association (Std. No. 321-1973). Both the liquids and resultant polymers are combustible. These adhesives should not be used near sparks, heat, open flames, or in areas of acute fire hazard. The highly exothermic polymerization that can result from the direct addition of alcohols, bases including weak amines, water, or surface activators should also be avoided.

Uses

2-Cyanoacrylic esters are used in so many different applications that it is virtually impossible to list them. Industrial product assembly applications include appliances, automotive, electronics, jewelry, hardware, sporting goods, instruments, tools, toys, computers, and many other items. These adhesives are also used in the repair of many rubber, plastic, and metal items in both industrial and consumer areas. The adhesives are used by morticians to seal eyes and lips. Police are using them to develop fingerprints (40). In other parts of the world, 2-cyanoacrylic esters are used in medicine and dentistry to achieve anastomosis and hemostasis. The ability of these materials to give strong bonds rapidly on almost any substrate from steel to skin has set the 2-cyanoacrylic esters apart from other adhesives and has enabled them to serve a broad and unique market.

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